REMARKS/ARGUMENTS

Claims 1, 22, 23, and 24 are pending. Claims 2-22 have been cancelled without prejudice.

Claims 1 and 23 have been amended to recite that the method occurs in an admixture in an admixture comprising a cell-extracted microsome fraction, NADPH, palmitoyl CoA, and labeled malonyl-CoA. Support for this amendment can be found on page 11, lines 1-7. The claims were further amended to recite that the LCE is a long chain fatty acyl elongase.

Claims 22 and 24 have been amended to recite that at least 20 % of the LCE is inhibited. These amendments are supported by the specification, such as page 10, lines 17-21, page 11, lines 8-12,, which states "When the expression level of LCE gene or a gene which is functionally equivalent to LCE gene is reduced by at least 20% and preferably at least 50% after administration of or contact with the test compound compared to the level before administration of or contact with the test compound, the test compound may be evaluated as a compound effective for treatment or prevention of obesity," and page 26, lines 1-9, which states "FIG. 5(a) is a graph showing LCE mRNA expression, and FIG. 5(b) is a graph showing elongation activity. As seen in FIGS. 5(a) and (b), it was confirmed that LCE expression had been specifically inhibited and that LCE activity had also been inhibited."

It is believed that the above amendments do not introduce new matter into the application.

I. Claim Rejection – 35 U.S.C. § 112

Claim 24 has been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite because the rejection states that Claim 24 does not further limit Claim 23 from which it depends.

Claim 24 has been amended to recite that the method of Claim 23 wherein the test compounds which inhibit at least 20 % of the activity of LCE activity are selected. Currently amended Claim 24 is believed to further limit Claim 23. In light of the amendment, reconsideration of the rejection is requested.

II. Claim Rejection under U.S.C. § 102(b)

Claims 1 and 22-24 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Berghs et al. (WO2004/013347). The rejection states "Berghs et al (WO 2004/013347) teach methods of evaluating compounds that are effective for treating comprising contacting an LCE protein with a test compound, as well as contacting LCE with a test compound in the presence of a plurality of elongase proteins, and selecting the test compounds

that inhibit LCE activity (see abstract, pages 5-9, 14, 17-18, and claims 1, 2, 6, 11-13, 17-19, 24, 25 and 28; SEQ ID No. 17, encoding SEQ ID No. 18)."

The applicants respectfully disagree with the rejection on the grounds that Berghs fails to teach or suggest each and every element of the claimed invention. For a prior art reference to anticipate a claimed invention, the prior art reference must teach each and every element of the claimed invention. *Lewmar Marine v. Barient* 827 F.2d 744, 3 USPQ2d 1766 (Fed. Cir. 1987).

The applicants' currently pending claims are drawn to methods for identifying inhibitors of LCE activity in an assay in which the LCE is in an admixture comprising a cell-extracted microsome fraction, NADPH, palmitoyl CoA, and labeled malonyl-CoA Berghs discusses assays for identifying inhibitors of LCE, for example, Berghs states on page 179, lines 20-22, "In a screening assay for inhibitors of LCE, radiolabelled malonyl-CoA plus palmitate will yield radiolabelled stearate that can be detected by partition assay." Bergh further provides on page 195, beginning at line 9, a brief discussion entitled "Assays Screening for Modulators of Long Chain Fatty Acyl Elongase" and states that potential methods for Measurement of Fatty Acyl elongation reaction in microsomes are described by Nagi et al. . . ., and by Moon et al...." However, Berghs does not specifically disclose an assay that uses an admixture comprising a cell-extracted microsome fraction, NADPH, palmitoyl CoA, and labeled malonyl-CoA to identify inhibitors of LCE. Berghs' assay appears not to include NADPH and as such, does not teach each and every element of the currently claimed method.

In addition, Berghs states on page 195, lines 28-31, that their "results indicate that a modulator of Long Chain Fatty Acyl Elongase activity, such as an inhibitor, activator, antagonist, or agonist of Long Chain Fatty Acyl Elongase may be useful for treatment of such disorders as obesity . . . ." Because this statement appears to include all possible outcomes as desirable, this statement suggests that Berghs did not know what the desired outcome of the assay should be. This attempt to cover all possible outcomes for the assay suggests that Berghs does not teach an assay that includes each and every element of the currently claimed method.

In light of the above, it is believed that Claims 1 and 23 are novel over the prior art. Reconsideration of the rejection is requested.

II. Claim Rejection under U.S.C. § 103(a)

Claims 1 and 22-24 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Moon et al. (J.Biol. Chem. 276: 45,358-45,366 (2001) in view of Matsuzuka et al. (J. Lipid Res. 43: 911-920 (2002).

The applicants respectfully disagree. The prior art (Berghs, Moon, and Matsuzaka) does not disclose nor suggest the applicants discovery, "a fixed correlation between weight change and LCE expression," that is, they do not disclose any data which directly indicate a connection between LCE expression and obesity.

Berghs observed decreased LCE expression in the brown adipose cells of obese mice and no alteration of LCE expression in the white adipose cells in the mice. In light of the observation, Berghs suggests a method of identifying compounds that modulate LCE activity. However, Berghs does not disclose nor suggest any correlation between weight change and LCE expression/activity in mice, much less any connection between LCE and obesity.

Moon observed an increase in expression of LCE in SREBP transgenic mice. They concluded from the observation that mouse LCE expression is increased by SREBPs. Moon also observed that cells over expressing LCE showed increased fatty acid elongation activity and concluded from the observation that LCE has a role in the mammalian elongation system that converts palmitic to stearic acid. Moon further observed that LCE mRNA is highly expressed in liver and adipose tissue, but does not disclose nor suggest that they observed any correlation between weight change and LCE expression/activity in mice, much less any connection between LCE and obesity.

Matsuzaka observed that cells over expressing LCE showed high activity of fatty acid elongation and also observed increased LCE expressions in the liver of SREBP transgenic mice and that XLR agonist, including SREBP expression, increased hepatic LCE expression. From these observations, Matsuzuka concluded that expression of LCE is regulated by SREBP. Matsuzka also observed induced expression of LCE in the liver of obese mice (ob/ob mice) but they do not disclose nor suggest any correlation between weight change and LCE expression/activity in mice, much less any connection between LCE and obesity.

The applicants show that there is a fixed correlation between weight change and LCE expression. The applicants provide data in which suppression of LCE expression led to a reduction of body weight, that is, reduction f fatty synthesis and cellular fat mass. Such data directly indicates a connection between LCE and obesity. For example, Fig. 11, which confirmed that administration of siRNA for LCE to mice reduced body weight and in addition and confirmed on the individual level that siRNA for LCE suppress LCE activity and exhibits an improving effect on obesity (Fig. 11 described on page 30, lines 6-11); Fig. 13, which confirmed that suppression of LCE expression by transfection of siRNA reduces fatty acid synthesis ability and triglyceride synthesis ability (Fig. 13 described on page 34, lines 11-13); and Fig. 19(c),

which confirmed that suppression of LCE expression by administration of LCE RNAi suppresses fat accumulation in liver during onset of obesity (described on page 38, lines 12-14).

Berghs, Moon, or Matsuzaka separately or together do not disclose or suggest such a correlation. They merely disclose the observation that increased LCE expression was observed in SREBP transgenic mice or obese mice. This alone does not suggest that there is a fixed correlation between weight change and LCE expression as disclosed by the applicants. Over expression of a gene in adipose cells of obese mice does not necessarily mean that such a gene is related to obesity, much less that suppression of such gene would effect a reduction in body weight. While many genes have been shown to have increased expression in the liver of obese mice (*See*, for example, Exhibit A: Ferrarante et al. Diabetes 50: 2268-2278 (2001)), it has also been shown that genes having high level increased expression do not necessarily have an affect on body weight (for example, Exhibit B: Weinstock et al., J. Lipid Res. 38: 1782-1794 (1997), Exhibit C: Brachvogel et al., Mol. Cell Biol. 23: 2907-2913 (2003)). In light of the above, the prior art does not suggest a fixed correlation between LCE expression and activity and obesity. Thus, the currently claimed method is believed to be unobvious over the prior art.

In view of the foregoing amendments and remarks, it is believed that the claims are in proper condition for allowance. Accordingly, Applicants respectfully request that a Notice of Allowance be forwarded to the Applicants. The Examiner is invited to contact Applicants' Attorney at the telephone number given below, if such would expedite the allowance of this application.

Favorable action is earnestly solicited.

CONDITIONAL PETITION

Applicant hereby makes a Conditional Petition for any relief available to correct any defect in connection with this filing, or any defect remaining in this application after this filing. The Commissioner is authorized to charge deposit account 13-2755 for the petition fee and any other fee(s) required to effect this Conditional Petition.

Respectfully submitted,

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